

AMENDMENTS TO THE CLAIMS

Claims 1-11 (Canceled).

12. (Currently amended) An isolated polynucleotide encoding the alpha chain portion as defined in claim 1 a T cell receptor (TCR) alpha chain portion containing three complementarity determining regions (CDRs):

CDR1 α : SSYSPS (SEQ ID NO: 2);

CDR2 α : YTSAATL (SEQ ID NO: 3); and

CDR3 α : SPFSGGGADGLT (SEQ ID NO: 5),

or encoding a modified TCR alpha chain portion wherein up to three amino acid residues in one or more of the CDRs are replaced by another amino acid residue, wherein a TCR containing the modified TCR alpha chain portion encoded by the said polynucleotide, and a TCR beta chain portion containing three CDRs:

CDR1 β : DFQATT (SEQ ID NO: 6);

CDR2 β : SNEGSKA (SEQ ID NO: 7); and

CDR3 β : RDGGEGSETQY (SEQ ID NO: 9),

has a greater affinity for an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex than a TCR containing the unmodified TCR alpha chain portion.

13. (Currently amended) An isolated polynucleotide encoding the beta chain portion as defined in claim 1 a T cell receptor (TCR) beta chain portion containing three complementarity determining regions (CDRs):

CDR1 β : DFQATT (SEQ ID NO: 6);

CDR2 β : SNEGSKA (SEQ ID NO: 7); and

CDR3 β : RDGGEGSETQY (SEQ ID NO: 9),

or encoding a modified TCR beta chain portion wherein up to three amino acid residues in one or more of the CDRs are replaced by another amino acid residue, wherein a

TCR containing the modified TCR beta chain portion encoded by the said polynucleotide, and a TCR alpha chain portion containing three CDRs:

CDR1 α : SSYSPS (SEQ ID NO: 2);

CDR2 α : YTSAATL (SEQ ID NO: 3); and

CDR3 α : SPFSGGGADGLT (SEQ ID NO: 5),

has a greater affinity for an HLA-A2/ RMFPNAPYL (SEQ ID NO: 1) complex than a TCR containing the unmodified TCR beta chain portion.

14. (Currently amended) An isolated polynucleotide encoding the single chain TCR molecule as defined in claim 7 a single chain TCR molecule containing an alpha chain portion and a beta chain portion,

wherein the alpha chain portion contains three CDRs:

CDR1 α : SSYSPS (SEQ ID NO: 2);

CDR2 α : YTSAATL (SEQ ID NO: 3); and

CDR3 α : SPFSGGGADGLT (SEQ ID NO: 5),

and wherein the beta chain portion contains three CDRs:

CDR1 β : DFQATT (SEQ ID NO: 6);

CDR2 β : SNEGSKA (SEQ ID NO: 7); and

CDR3 β : RDGGEGSETQY (SEQ ID NO: 9),

or encoding a modified single chain TCR molecule wherein up to three amino acid residues in one or more of the CDRs are replaced by another amino acid residue, wherein the modified TCR encoded by the said polynucleotide has a greater affinity for an HLA-A2/ RMFPNAPYL (SEQ ID NO: 1) complex than a TCR containing the unmodified CDRs.

15. (Currently amended) An expression vector comprising a polynucleotide according to any of claims 12 to [[15]] 14.

16. (Original) An expression vector according to claim 15 which is a retroviral vector.
17. (Currently amended) A host cell comprising a polynucleotide according to any of claims 12 to 14 ~~or an expression vector according to claims 15 or 16.~~
18. (Original) A host cell according to claim 17 which is a T cell.
19. (Original) A host cell according to claim 18 which is a T cell derived from a patient.
20. (Withdrawn, Currently amended) A method of combating a WT1-expressing malignancy in a patient, the method comprising introducing into the patient a T cell, preferably derived from the patient, which is modified to express ~~the TCR molecule of any of claims 1 to 11~~ the polynucleotide of any of claims 12 to 14.
21. (Withdrawn, Currently amended) A method according to claim 20 comprising (1) obtaining T cells from the patient, (2) introducing into the T cells a polynucleotide according to any of claims 12 to 14 ~~or an expression vector according to claims 15 or 16~~ so that the T cell expresses the encoded TCR molecule and (3) introducing the cells from step (2) into the patient.
22. (Withdrawn, Currently amended) A method according to claim 20 ~~or 21~~ wherein the WT1-expressing malignancy is any one or more of breast cancer, colon cancer, lung cancer, leukaemia, ovarian cancer, melanoma, head and neck cancer, thyroid cancer, glioblastoma and sarcoma.
- 23-24. (Canceled)

25. (Withdrawn, Currently amended) A method of selecting a TCR molecule with improved binding to an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex comprising (a) expressing the polynucleotide of any of claims 12-14 providing a TCR molecule containing an alpha chain portion and a beta chain portion wherein the alpha chain portion contains three complementarity determining regions (CDRs): CDR1.alpha.: SSYSPS CDR2.alpha.: YTSAATL CDR3.alpha.: VVSPFSGGGADGLT or comprising or consisting of SPFSGGGADGLT and the beta chain portion contains three complementarity determining regions (CDRs): CDR1.beta.: DFQATT CDR2.beta.: SNEGSKA CDR3.beta.: comprising SARDGGEG or comprising or consisting of RDGGEGSETQY, wherein at least one amino acid residue in one or more of the CDRs as given is replaced with another amino acid residue, (b) determining whether the TCR molecule expressed by the polynucleotide of any of claims 12-14 binds to an HLA-A2/RMFPNAPYL HLA-A2/ RMFPNAPYL (SEQ ID NO: 1) complex with greater affinity than a TCR molecule without the replacement amino acid(s), and (c) selecting a polynucleotide encoding a TCR molecule which binds with greater affinity to the HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex.

26-27. (Canceled)

28. (New) A host cell comprising an expression vector according to claim 15.

29. (New) A host cell according to claim 28 which is a T cell.

30. (New) A host cell according to claim 28 which is a T cell derived from a patient.

31. (New) A method of combating a WT1-expressing malignancy in a patient, the method comprising introducing into the patient a T cell modified by the expression vector of claim 15.

32. (New) A method according to claim 31 wherein the WT1-expressing malignancy is any one or more of breast cancer, colon cancer, lung cancer, leukaemia, ovarian cancer, melanoma, head and neck cancer, thyroid cancer, glioblastoma and sarcoma.